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The Pediatrician and the Public School

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Dr. Clark:

This program has been arranged to introduce the pediatrician to one of the many facets of community health which should be considered necessary to the establishment of a well-rounded pediatric training program. This, we hope, will be an example of the multidisciplinary approach to problems which concern the pediatrician and the community alike.

At the turn of this century the delivery of the newborn infant was moved from the home to the sterility of the hospital; unfortunately, at about the same time we also began moving toward a sterility of relationships. The cycle is now being completed; the "New Pediatrics" which we read about so much these days is merely the old art of interpersonal relationships as well as the acceptance of community responsibilities often lacking in the professional life of today's physician.

Dr. Hansen:

It is very gratifying for us in the Department of Education to know that the medical profession, particularly the pediatrician, is concerned with total care of the child; this, of course, includes not only the physical needs of the child, but also his emotional and social needs. All these are necessary to understand him as a person living in a given environment, and in so doing to work with him more effectively.

This is exactly what the philosophy of public education has been during recent years. If we are to do a better job of educating the child, we must recognize him as a person to be educated in the broad sense of the word. We must understand him as an individual living in a home and a community, having certain physical, emotional, and psychological characteristics, and responding, as a result of combinations of these characteristics, in certain ways in the classroom setting.

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There is a very close relationship between health and educability. For example, we are quite sure that many of our problems in reading result from vision impairment. Despite all that we attempt to do to discover these deficiencies and to correct them, there are undoubtedly many who are going through school, stage by stage, with visual handicaps. These children are thus not able to respond to educational opportunities to the extent that they would if there were a sure way of recognizing their health problem. Another problem is the hungry child; the hungry child is a child who does not respond well to education.

These are illustrations of the problems that we must deal with if we are going to provide a maximal educational effort for children. We must know about their health problems and we must make as great a contribution as we can to the solution of these health problems in cooperation with the professional experts in this field, the physician, both public and private. For this reason it is always desirable for representatives of education and medicine to sit down together to relate their programs to the child's needs and approach these problems together as a team.

A second and very important aspect of our responsibility has to do with instruction in health. This has long been recognized as a curriculum responsibility, and all educators have a concern for education which will lead to improved health practices by children coming into the schools.

There are numerous questions which arise in conducting a comprehensive school health program. For example, how can we get help from the family physician when so many of our children do not have a family physician to go to? It must be understood that there are many children in our schools who rarely see a physician on a private basis. These children have none of the permanent relationships which children in more favored families may have; they do not have a pediatrician who is concerned with their development from the period even prior to birth to the age of 12 and beyond. What should we do to help make it possible for more families, even those who can afford to do so, to establish a relationship with the physician who can then take a more or less continuing interest in the total development of the children? This is one of the major problems.

Next, can we as school people consult directly with the family physician or must we go through the parents? What is the responsibility of the family physician in respect to this relationship? If , for example, we are having a problem with a child who seems to be in ill health, and, if we know that there is a family physician, can we, or should we, ask the teacher, the counselor, or the nurse to call the physician to report and consult? If there is difficulty requiring a teamwork consultation about a child who is in need of help, can we invite that child's family physician, the pediatrician, into the conference? Would this be done on a fee basis, and would the pediatrician

respond? The assumption is that this procedure would be a good thing if it could be done. We in the school system feel that if we bring the family physician into the team operation on behalf of the child who needs special attention, we will do a better job of education. The physician himself would also be more secure in his treatment of such a child whom he had observed in the school setting.

Another question which has been raised in some publications recently is whether the pediatrician can be depended upon to respect the professional standing of teachers and school officials. Do these two disciplines coordinate, do they work together on an equal plane, or is there a tendency on the part of the pediatrician to consider the opinions and judgments of the professional teacher as being suspect, as not having the same level of respectability as his own? This is of some concern since there is sometimes a tendency to approach a common problem with an unbalanced relationship, and we must come to the point where teachers and pediatricians and counselors and principals can talk together in a person to person relationship with mutual confidence and respect as to judgment.

Should the pediatrician report defects to the school? Should the physician who knows the child as a total personality let those of us in the school know if there are findings which may affect his responses to the school setting? If this is done, how should it be done? Should it be by written communication? What about clearance with the parents? These are questions of real significance from the practical point of view. And yet how wonderful it would be if when a pediatrician, for example, finds the beginning of a hearing impairment in a child, it could be reported to the school authorities immediately so that the teachers would be informed, rather than to have to wait until a crisis occurs and the impairment is discovered through the accident of observation. If we can find the processes by which these communications can be delivered back and forth, the schools could do a much better and more efficient job with the children.

If parents ignore reports of health defects, what is the school's position? We oftentimes find it within our resources through the work of nurses and physicians to identify many defects, the treatment of which is not followed through, in part because we do not have the resources, either through public or private means, to send people into the home to help parents arrange for correction of these defects. The result is that we do only half a job in too many instances.

And finally: Should a physical examination be required of every school entry; should these be periodic; and to what extent should the family physician be a part of the process? At the moment the only required examination for admission to school is a certificate of vaccination. We do not require a general physical examination as a condition for admission to school.

Many believe we should. This could be done either on the basis of a conference with the parents to persuade them that this is wise to do, or if not, make the examination a statutory requirement.

Dr. Finucane:

In any discussion of the health services available to the school child in the District of Columbia, and how the private practitioner participates in these services, it should first be pointed out that it is possible to find any type of plan for a school health program in any one of a number of cities and communities around the country. Of these, it can be said truthfully that there is no ideal or set pattern which will be the best pattern to meet the needs of every community; each community must develop its own plan of procedure and follow it to meet its own needs.

There are roughly 140,000 small children under the supervision of over 6,000 teachers in the District of Columbia in some 200 school buildings located in all parts of the city. While the primary purpose of the schools is to educate these children, it is also their responsibility to supervise the care, well-being and safety of these children for five hours a day on the 180 days of the year in which they are attending school. Experience has shown that the collection of large numbers of children in confined quarters such as school buildings is conducive to certain health and safety hazards. Experience has also shown that undetected health defects impair the learning ability of the child. To deal with these situations in an effective manner, a program of health services has been developed jointly by the school system and the Department of Public Health, utilizing personnel from these two agencies as well as private physicians and other health resources in the community. These health services are voluntary insofar as parents are concerned, with certain exceptions that relate to the control of communicable disease.

The health services provided in the schools fall into three main categories: general health screening, control of communicable disease and first aid and emergency care. Other health services of lesser scope are also provided.

The general health screening consists of several items: height and weight measurements and dental and vision screening of all children, screening of hearing of children in selected grades, and general medical screening by physicians of children new to the school system, those referred on the basis of teacher observation and teacher-nurse conference, and those in classes for the handicapped. Children who are new to the school system are encouraged to have their medical screening done by their own physician when they have one. These examinations in the schools are not definitive diagnostic examinations; their purpose is to identify children with suspected

or actual health defects. It is characteristic of these screening health examinations to yield a high rate of over-referrals. For example, experience shows that of the children who fail the vision screening test, some 50 per cent have nothing wrong with their eyes, and only 30 per cent require glasses.

The control of communicable diseases includes the requirement of smallpox vaccination prior to school entry, provision of booster immunization against diphtheria, pertussis and tetanus in the kindergarten, junior primary and first grade, provision of booster immunization against poliomyelitis, daily teacher observation of all pupils for the early detection of suspected communicable disease and the exclusion of pupils from school. Screening for ringworm of the scalp in selected schools and tuberculin skin testing on a periodic basis is also carried out.

First aid and emergency care are the responsibility of school personnel. The school physician and public health nurse are available as resource people. The teacher is required to have for each child a record on how to reach the parent or other responsible adult when needed. The central office of the School Health Service is also available for advice and assistance in emergency.

The detection of children with suspected or actual health defects is not an end in itself but is merely a first step toward getting these defects diagnosed and corrected. Hence a major effort of school and health department personnel is the counseling of the parents of children with health defects regarding these defects, an intensive follow-up to insure that such children receive needed medical care, and seeing that reports of the findings are returned to the school. Children in need of medical care are referred to their private physicians, and, when they do not have private physicians, to hospital clinics, health department clinics and other medical resources in the community. Diagnostic and treatment facilities are not provided in the schools except in limited areas such as the dental clinics, and the physical therapy and occupational therapy in the C. Melvin Sharpe Health School.

It is estimated on the basis of available data that approximately 50 per cent of school children in the District of Columbia cannot routinely afford private medical care, that 10 per cent are marginal in this respect, and that only 40 per cent routinely use private medical care. Hence, it has been necessary for the Health Department to develop its own diagnostic and treatment clinics for school children. These include dental clinics, eye clinics, a hearing clinic, pediculosis clinic, ringworm clinic, and child guidance clinic in addition to other existing facilities.

While the health defects of most children can be corrected more or less completely, and such children can fit into regular class schedules, there

remain a significant number of children who require special handling in the school because of residual handicaps of a temporary or permanent nature. They may need nothing more than a rest period during the day or favored seating in a regular class, or they may need to be placed in a special class, a special school or on home instruction. Children being considered for special placement are referred to the Medical Evaluation Clinic in the District of Columbia Health Department for review or further study as the circumstances may warrant. The school system has found this desirable so that medical reports of a complex nature can be interpreted to them and recommendations can be made on the basis of more intimate knowledge of the special facilities available. The final decision as to placement is the responsibility of the school system. Children in special classes or special schools are re-evaluated each year to determine whether special placement is still indicated.

The private physician participates in the general medical screening of pupils new to the school system. He also immunizes school children under his care, diagnoses and treats those patients who are referred to him by the School Health Service for suspected or actual health defects and advises the School Health Service of the special needs of his patients with respect to schooling and school placement.

The law requires every child to be protected against smallpox prior to school enrollment; exceptions have to be authorized by the central offices of the School Health Service and are based on personal inspection and a written statement from his doctor. The child who has been excluded from school because of ringworm of the scalp cannot return to school without a certificate from the Health Department. The child with impetigo, scabies and ringworm of the skin is subject to examination by the school physician before readmission to school; usually, however, a written note from his doctor will suffice. Recommendations from a physician requesting that a child be excused from certain physical activity or that he be returned to full activity are honored by school personnel. Occasionally there is reason to question such a recommendation, and the matter will be referred to the school physician. When there is a difference of opinion it is the policy of the school physician to contact the private physician regarding the situation. Rarely a school physician will be remiss in calling the private physician and has to be reminded that the above policy is still in effect.

Children who fail the screening examinations in school are referred to their own doctors for definitive diagnosis. Frequently the doctor will find nothing wrong with the child. An excellent statement on how to handle the situation with the parents has been prepared by Dr. Scobee.[1] He was speaking of vision screening failures, but the statement applies equally well to other screening failures:

The manner in which we tell the parents that there is in fact no defect can affect their subsequent attitude toward not only the school and the school nurse but toward ourselves as oculists.

If the information is given in an abrupt, gruff, "I'm-too-busy-to-be-bothered-with-cases-where-nothing-is-wrong" manner, the reaction of the normal parent is to accept the ophthalmologist's word and then condemn the school nurse or teacher. After a day or two the experience will often begin to rankle in the mind of the parent, and frequently there is a turning against the ophthalmologist too—partly because a fee was charged when nothing was found to be wrong. This is of course illogical but is nevertheless the way that many persons react. If at some future date something is actually wrong with the child's health during a school examination, a note sent home to the parents is likely to be ignored as "another false alarm."

How much better is the entire situation if the ophthalmologist informs the parent that nothing is wrong in a manner something like this: "You are fortunate in two ways. In the first place a careful examination has revealed that there is nothing seriously wrong with your child's eyes, and that whatever it was that made the school nurse or teacher suspicious must have been temporary. In the second place you are fortunate to have your child in a school where some attention is paid to more than mere books. The school is apparently interested enough in your child to examine him and, at the time of the examination, his eyes didn't seem to be normal."

The response of the average parent to this type of reasoning is almost invariably good.

I hope that this general description of the content of the School Health Service and of some of its procedures will contribute toward improving mutual understanding between the private physicians and the School Health Service.

Dr. McLendon:

There are two areas of activity present in a good school health program to which the physician caring for children can contribute. First, he can cooperate with school authorities in providing information concerning children seen in his private practice; second, he can directly assist by work in clinics and programs designed to reduce physical and behavioral problems. The physician stands at the crossroads of diagnosis and later management; whether he functions in the school setting itself or functions as the child's physician, his background of education and training certifies to this status.

In his private practice the children's doctor has taken care of the illnesses and problems incident to the school-age child's infancy and preschool development. He is familiar with the family economic, cultural and social environment, as well as the personalities of the parents and siblings. When the early school-age youngster is reported to be showing emotional

deviations and asocial behavior, no one is in a better position to aid the parents and the school than he. Thus requests for information as well as cooperation in conferences with parents and teachers should be generously provided; he may supplement his clinical interpretation with laboratory and psychological data. This role of the physician is not only a privilege but a responsibility; he should at the same time recognize his limitations.

The health and well-being of the indigent child is primarily a responsibility of the personnel of the Health Department and School Administration. With these children the nurse, social worker and counselor are brought into the picture much earlier. They must furnish the socio-cultural background of which the physician has no knowledge. With this knowledge he is fortified to stand as the director of further investigation and management.

It is the additional responsibility of either the private or public health physician to recognize, particularly in the elementary school-age child, such physical and physiological handicaps as genetic abnormalities, birth injuries and other acquired handicaps, mental retardation, metabolic deviations, subnormal sight and hearing, speech defects, etc. and correct them to an optimal level before an emotional or behavioral problem superimposes.

The tremendous increase in the school population, the crowded classrooms, the problems of cultural and ethnic admixture, family irresponsibility and community disorganization place a burden on present school personnel unprecedented in the past. In many of these areas are opportunities for the physician to participate in educational programs of a civic nature. Acceptance of these responsibilities is part of the broadening horizon of pediatric practice.

Dr. Hobart:

The private physician has a responsibility to the community as well as to the individual patient in school health affairs. The community looks to the private physician for leadership. Those who are working in the field of education have expressed a desire for more active participation by the physician in health education and physical education matters. School health should be regarded as an interesting field of medical endeavor; a child's health and general well-being are important if he is to attain the academic standards that are set up for him. The more thorough knowledge and appreciation of growth and development and the increase and shift in population have done much to arouse interest in school health.

How can we as private physicians best serve our community and our patients in relation to school health? This is a question of great magnitude. Much ground work has been done. We must pause to recognize the efforts of part-time school physicians and physician-members of the Sub-committee of Child Welfare of the District of Columbia Medical Society; all these have made great contributions to local school health. What can the remainder of us do?

First, to do a good job for ourselves and our patient, we should keep ourselves informed on school health matters. Reports of the Conference on Physicians and Schools, health policies of the Academy of Pediatrics, reports of the American Public Health Association, and literature from the Office of Health, Education and Welfare are all available and informative. The establishment of extension courses for physicians in school health has been suggested, and should be considered and encouraged. The establishment of clinics for the school-age child in our hospitals should be considered. The physician's evaluation of the school-age child should be meaningful to both the parent and the school.

Second, the private physician should endeavor personally to strengthen his lines of communication to the school. He must remember that communication is a two-way street and his personal effort will encourage an effort in return by the school. The success or failure of a school health program hinges largely on communications.

Third, the physician should acquaint himself with school curriculum and school administration. This would enhance his ability to advise in health education and physical education. It would also give him a better understanding of the problems of his patients who are school-age children.

Fourth, the private physician should make himself available and accept the responsibility of serving in consultation with the school physician, nurse or teacher.

Fifth, he should accept the present-day challenge to the practitioner, in the light of newer concepts of medicine, to improve the relationship with the schools. Every effort should be made by the local medical society to keep its membership informed on school health matters. This can be done by discussion groups and planning programs within the medical society. The problem of the school-age child is the concern of all physicians, but it is the special responsibility of those who have found themselves involved and who are interested in school health to make every effort to acquaint the whole profession with the problems of the school-age child.

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Sex Chromatin Patterns and Ultimate Sex Determination

PACITA PRONOVE, M.D.*

Experiments done in the embryology of lower vertebrates have demonstrated that the "differentiation of the embryonic gonad is not irrevocably prefixed by the genetic constitution," but may also be affected by external factors.[1] From these experiments have evolved two basic principles.[2] The first of these is that "both the embryonic gonad and the secondary sex apparatus have the ability to differentiate oppositely to the genetic sex constitution." In other words, the genetic male can develop ovaries and the genetic female can develop testes if there is a proper hormonal or physical influence exerted while the embryonic gonad is in the indifferent state. The other principle that has evolved from these experiments is concerned with the retention of the bipotentiality of the germ cells in spite of their genetic constitution, e.g., the male germ cells can differentiate as ovogonia, undergo ovogenesis, and produce functional ova.

In the embryogenesis of secondary sex organs the secretions of the embryonic gonad determine the differentiation of most secondary sex characters, a process which is not under direct genetic control; this is exemplified by Jost's experiments of intrauterine castration of rabbit fetuses.[3] This principle was confirmed by culturing the embryonic sex primordia of rats *in vitro*.[4] In these experiments, neither ovaries nor testes were developed; there was regression of the mesonephric duct, and female secondary sex structures (Müllerian duct derivations and external genitalia) resulted, "indicating the need for the inductive influence of the fetal testes to produce a male-type development in rats and rabbits, whereas the female secondary sex characteristics require only neutral conditions." However, not all secondary sex characters are controlled by gonadal influences. Some differentiate according to genetic constitution regardless of functional sex; examples of this are found in birds[5] and the opossum.[6]

Barr and his associates,[7, 8] in their study of the nuclear morphology of neural cells in the cat, first discovered that sexual dimorphism was present; this permitted the identification of whether the tissue was of male or female origin. When this study was extended to several mammals, including man, it was found that the characteristic chromatin masses which are absent or only occasionally seen in male cells were present in female tissue (fig. 1). This can be demonstrated in man in the skin,[9] leukocytes,[10] buccal mucosa,[11] and vaginal exfoliate cells[12] (table 1).

The characteristic chromatin mass is postulated to represent a fused

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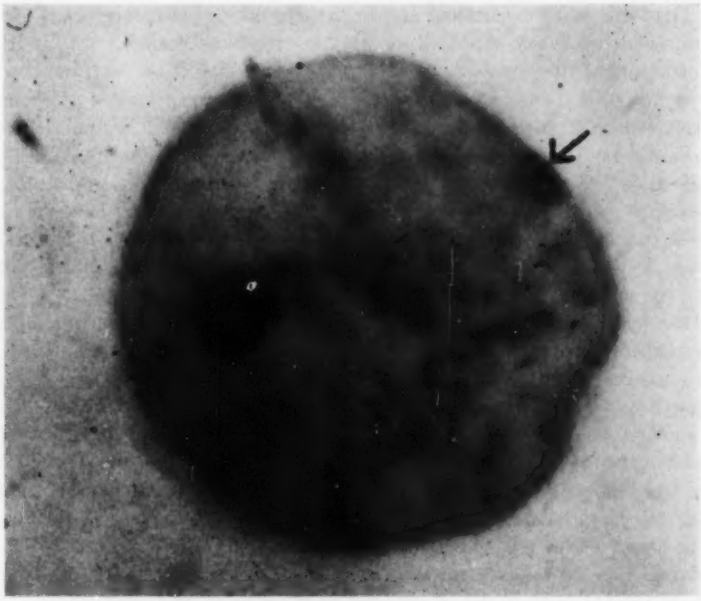

FIG. 1. Cell nucleus showing sex chromatin mass attached to the inner surface of the nuclear membrane (arrow). This formation is characteristic of tissue cells of genetic females (see table 1 and text).

heterochromatic region of the XX sex chromosomes; this fusion presumably does not occur in the XY sex chromosome pair of the male so that a similar structure is not visible.[13, 14] On this basis it appeared reasonable to the investigators of this fascinating phenomenon to relate nuclear morphology to genetic sex. Table 1 illustrates the correlations obtained in one series in differentiating between the normal male and the normal female sex by the use of both the skin biopsies and the buccal mucosal smears.

TABLE 1

Reliability of Buccal Mucosal Smears and Skin Biopsy Specimens in Determining Genetic Sex[2]

Tissue	Sex	Number of Cases	Average Percentage of Positive Nuclei and Range
Skin	Male	90	4.7 (1–12)
	Female	74	69.0 (51–82)
Buccal Mucosa	Male	146	0.7 (0–4)
	Female	93	53.0 (20–79)

That this is all theoretical and that there is no convincing proof for the chromatin mass-sex chromosome relationship was pointed out by Barr. In support of this contention, however, Segal and Nelson[2] summarized the evidence as follows: 1) Characteristic heteropyknotic bodies are seen in greater than 50 per cent of nuclei of normal female cells; 2) similar heteropyknotic bodies are seen in less than 5 per cent of normal male cells; 3) this mass reacts strongly in a positive manner with Fuelgen stain and therefore is regarded as a heterochromatic material; 4) the chromatin mass can be identified with its characteristic sex distribution in the embryo; 5) the mass is not influenced by exogenous hormone administration nor by an abnormal endogenous hormonal status; 6) the mass is unaffected by castration; and 7) the mass is present from the embryonic stage onward until death. From these above observations the chromatin mass was assumed to be a "genetically determined marker of epistatic sex, regardless of direction taken in the apparent sex differentiation."

In the study of the relationship of the sex chromatin mass and chromosomal loci the following principles are involved, as reviewed by Segal and Nelson:[2] 1) Female and male genetic sex determiners are present in both sexes; each sex has a potentiality for the other sex; 2) maleness or femaleness is dependent on the existence of a quantitative relation or "balance" between the two types of sex determiners; 3) the determiner of the human female sex is located within the X chromosome, whereas the determiner of the human male sex lies outside of the X chromosome; 4) the male sex determiner lying outside the X chromosome in humans may occur on the Y chromosome or on a pair of autosomes; and 5) the "balance" system works so that two doses of female determiners in the X chromosome (XX in this case) dominate the male determiner outside the X, but one dose (XY) is insufficient for dominance of female factors. Relating the chromatin mass to the autosomes rather than to the X chromosomes was suggested simply to emphasize the equivocal nature of the chromatin mass-sex chromosome concept.

More recently, however, Tjio and Levan[15] and Ford and Hamerton[16] made a startling discovery that the total chromosome number of normal man is the diploid number 46 (44 autosomes and 2 sex chromosomes) instead of the diploid 48, a count we had erroneously believed for more than 30 years. The presence of the XX sex chromosomes in the normal female and of the XY sex chromosomes in the normal male were confirmed. These findings having inspired the search for aberrations in the chromosomal count of man, particularly in the case of human intersexuality where discrepancies occur between apparent or functional sex and the nuclear chromatin mass, led to some of the most exciting discoveries in the past year, the results of which are shown in table 2. It is apparent that a definite and positive cor-

TABLE 2
The Chromatin Mass and its Relation to the Sex Chromosomes

TABLE 2

The Chromatin Mass and its Relation to the Sex Chromosomes

Clinical Diagnosis	Phenotype	Barr's Chromatin Mass	Chromosomes				References
			Autosomes	Sex	Total Count	Tissue Source	
Normal	Male	−	44	XY	46	Lung fibroblasts and skin	Tjio and Levan[15]
Normal	Female	+	44	XX	46	Bone marrow	Ford and Hamerton[16]
Secondary amenorrhea (super female)	Female	+ (14% with double chrom. bodies)	44	XXX	47	Bone marrow and skin	Jacobs et al.[26] (1 case)
Congenital multiple vertebral anomalies and mentally dull normal	Male child	Not performed	43 (2 fused, T_1V_3)	XY	45		Turpin et al.[27] (1 case)
Testicular feminization syndrome (primary amenorrhea)	Female	−	44	XY	46	Bone marrow and skin	Jacobs et al.[28] (4 cases)
Turner's syndrome or gonadal dysgenesis	Female	−	44	XO	45	Bone marrow Skin Bone marrow Bone marrow	Ford et al.[17] (1 case) Tjio et al.[18] (1 case) Ford et al.[19] (1 case) Jacobs and Stewart[20] (1 case)
Klinefelter's syndrome	Male	+	44	XXY	47	Bone marrow	Jacobs & Strong[21] (1 case) Ford et al.[19] (4 cases) Stewart[22] (5 cases, 1 counted)
Mongolism	Female Male	+ −	44 + 1 44 + 1	XX XY	47 47	Bone marrow Conn. tissues	Jacobs et al.[23] (6 cases) Lejeune et al.[24] (3 cases)
Klinefelter's syndrome and mongolism combined	Male	+	44 + 1	XXY	48	Bone marrow	Ford et al.[25] (1 case)

relation exists between Barr's nuclear sex chromatin mass and the presence of a complete complement of XX sex chromosomes, irrespective of the presence or absence of a Y sex chromosome.

In Turner's syndrome where only 45 chromosomes (44 autosomes plus one X sex chromosome) are found,[17-20] the individual is a "half female" and definitely not a genetic male as it was considered to be up to one year ago. In the light of these findings there is a consensus that the nuclear sex chromatin mass should preferably be referred to and expressed in terms of positive or negative (Barr's test) instead of incorrectly identifying it with the genetic or chromosomal sex. With regard to the fewer cases of Turner's syndrome reportedly associated with a positive Barr's test, no reports of their chromosomal counts are as yet available.

Nondisjunction of the sex chromosomes at either mitosis or meiosis[17, 21] during gametogenesis in one or other parent has been offered as a likely explanation for some of these sex chromosomal anomalies. In any event, this fascinating field is now wide open for the study of some of the many unsolved problems involving the congenital anomalies and/or metabolic aberrations of man.

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Pipamazine,* A New Antiemetic

Leticia U. Tina, M.D.†

Nausea and vomiting is a symptom complex which results from a variety of disorders. The medullary vomiting center which controls all vomiting can be excited in any of the following ways: 1) by direct stimulation (e.g., a rise in cerebrospinal fluid pressure), 2) reflexly through afferent autonomic tracts (e.g. gastric irritation), or 3) by chemicals present in the blood stream capable of exciting the center (e.g. apormorphine).[1] The

* Supplied as Mornidine® by G. D. Searle & Company, Chicago.

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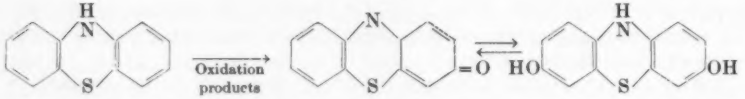
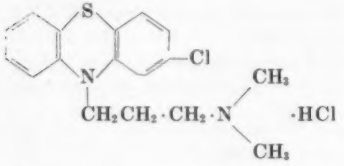
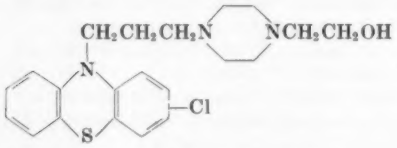
cause of vomiting is often easily ascertained, but at other times may be obscure. Regardless of the cause, certain harmful effects may follow when vomiting is persistent and severe. These include dehydration, hemoconcentration, peripheral circulatory collapse, alteration of the electrolyte balance, impairment of renal function, ketosis, acidosis in children and alkalosis in adults.

FIGURE 1

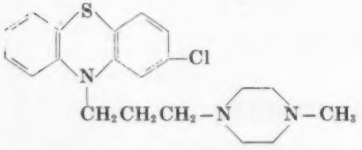




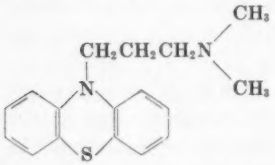
Chlorpromazine (10-[3-dimethyl amino propyl]-2-chlorophenothazine) (Thorazine)



Perphenazine (2 chloro-10-{3-[4-(β hydroxyethyl)piperazine]propyl}phenothiazine) (Trilafon)

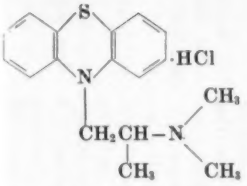


Prochlorperazine (2 chloro-10-[3-(1-methyl-4 piperazinyl)-propyl]-phenothiazine) (Compazine)

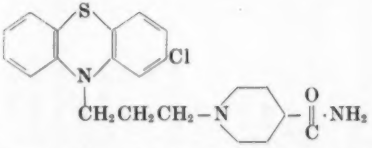


Promazine Hydrochloride (10-(3-Dimethyl amino propyl)-phenothiazine hydrochloride) (Sparine Hydrochloride)

FIGURE 1—*Continued*



Promethazine (N-(2'-dimethylamino-2'-methyl)-ethyl phenothiazine hydrochloride) (Phenergan)



Pipamazine (10-[3-(4-carbamoyl piperidino)-propyl]-2-chlorophenothiazine) (Mornidine)

Prior to the introduction of the phenothiazine derivatives as antiemetics, there were no satisfactory agents available for this purpose. The most common phenothiazine derivatives in current use are chlorpromazine (Thorazine®), prochlorperazine (Compazine®), perphenazine (Trilafon®), promazine hydrochloride (Sparine Hydrochloride®), and promethazine (Phenergan®). Their structural formulas are given in figure 1. These drugs are also effective tranquilizing agents and may be useful adjuncts in the management of emotional disturbances. It is of interest in this connection to note the anatomical proximity of the hypothalamus and the medullary vomiting center.

Phenothiazine, the parent compound, is oxidized and absorbed from the gastrointestinal tract,[2] and is excreted in the urine and bile. It is occasionally used as an antihelminthic, but extensive use is prohibited by its major toxic manifestation, red cell hemolysis. The antiemetic phenothiazine derivatives lack this toxicity but have certain untoward effects of their own. Hypotension, drowsiness, skin eruptions, fever and purpura may occur following their use.[3-6, 10] Agranulocytosis,[4, 7, 10, 11] although rare, has followed the use of chlorpromazine. Jaundice as a result of obstruction of intrahepatic biliary canaliculi is thought to be due to liver sensitization by chlorpromazine or prochlorperazine.[8-10] The jaundice is usually reversible, and no residual liver damage occurs. An increasing number of patients with extrapyramidal disturbances following use of chlorpromazine and prochlorperazine have been encountered.[4, 10, 12-14] One should be aware of the fact that these side effects may be shared by several of the phenothiazine derivatives because of their close chemical relationship. Continuous efforts to separate the undesirable effects from the therapeutic action are

TABLE 1

Pt.	Age	Sex	Weight Kg.	Diagnosis	History	Pipamazine	Results and Comments
L. F.	7½ y.	F	15	Reilly-Day Syndrome with pneumonia	Vomiting 2 days	5 mg p.o. q 4 h for four doses	Vomiting stopped, no side effects
J. C.	5 y.	M	28	Appendicitis	Vomiting 3 days	5 mg p.o. once	Vomiting stopped, no side effects
E. J.	3 y.	M	10	Mesenteric adenitis	Vomiting 1 day	5 mg p.o. once	Vomiting stopped, no side effects
B. T.	9 m.	F	5	Metastatic carcinoma	Nitrogen mustard 0.1 mg/Kg daily for one week	5 mg p.o. q 4 h for four doses	No effect
D. H.	5 y.	F	15	Pyelonephritis, azotemia	Vomiting 4 days	5 mg p.o. once	Vomiting stopped, slight drowsiness
C. S.	7 y.	F	14	Gastroenteritis	Vomiting 3 days	5 mg p.o. twice	Vomiting stopped, slight drowsiness
M. J.	6 y.	M	10	Acute pharyngitis	Vomiting 2 days	5 mg p.o. twice	Vomiting stopped
L. L.	4 y.	F	15	Cyclic vomiting	Vomiting 2 days	5 mg p.o. twice	No effect
J. K.	6 y.	M	30	Nephrotic syndrome	Nitrogen mustard 0.1 mg/Kg i.v.	None	Vomited 4 h. after med.
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	No vomiting
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	No vomiting
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	No vomiting felt drowsy
				Second series	Nitrogen mustard 0.1 mg/Kg i.v.	None	Vomited 5 h. after med.
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	Vomited 4 h. after med.
						5 mg i.m.	Vomiting stopped
					Nitrogen mustard 0.1 mg/Kg i.v.	10 mg p.o.	No vomiting
					Nitrogen mustard 0.1 mg/Kg i.v.	10 mg p.o.	No vomiting
R. K.	10 y.	M	55	Nephrotic syndrome	Nitrogen mustard 0.1 mg/Kg i.v.	None	Vomited 5 h. after med.
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	Vomited 4 h. after med.
					Nitrogen mustard 0.1 mg/Kg i.v.	10 mg p.o.	No vomiting
					Nitrogen mustard 0.1 mg/Kg i.v.	10 mg p.o.	No vomiting

E. W.	8 y.	M	29	Nephrotic syndrome	Nitrogen mustard 0.1 mg/Kg i.v.	None	Vomited 2 h. after med.
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	No vomiting
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	No vomiting
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	No vomiting
D. B.	4 y.	F	15	Nephrotic syndrome	Nitrogen mustard 0.1 mg/Kg i.v.	None	Vomited 3½ h. after med.
						5 mg i.m.	Vomiting stopped
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	No vomiting, slight drowsiness
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	No vomiting
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	No vomiting
K. A.	1 y.	M	8	Nephrotic syndrome	Nitrogen mustard 0.1 mg/Kg i.v.	None	Vomited 3 h. after med.
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg suppository	No vomiting or local eff.
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg suppository	Vomited 4 h. after med.
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	No vomiting
W. J.	6 y.	M	22	Nephrotic syndrome	Nitrogen mustard 0.1 mg/Kg i.v.	None	Vomited 3 h. after med.
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	No vomiting
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	No vomiting
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	No vomiting
H. G.	7 m.	F	9	Nephrotic syndrome	Nitrogen mustard 0.1 mg/Kg i.v.	None	Vomited 4 h. after med.
				BUN 48		5 mg i.m.	Vomiting stopped
					Nitrogen mustard 0.1 mg/Kg i.v.	5 mg p.o.	Vomited 2 h. after med.
					Nitrogen mustard 0.1 mg/Kg i.v.	10 mg p.o.	Vomited 3 h. after med.
					Nitrogen mustard 0.1 mg/Kg i.v.	10 mg p.o.	Vomited 1 h. after med.
E. A.	53 y.	M	77	Cerebral thrombosis	Vomiting 1 day	5 mg q 8 h p.o.	Stopped vomiting, no side effects
B. J.	15 y.	F	50	Azotemia—chronic pyelonephritis	Nitrogen mustard 8 mg/Kg i.v.; following day, second dose of nitrogen mustard	None	Vomited several times
						5 mg p.o.	Vomited, felt sleepy
C. H.		M		Meningitis	Vomiting 1 week	5 mg q 8 h p.o. for 3 days	Stopped vomiting, no side effects

TABLE 1—*Continued*

Pt.	Age	Sex	Weight Kg.	Diagnosis	History	Pipamazine	Results and Comments
E. T.	58 y.	M		Digitalis intoxication	Vomiting	10 mg i.m.	Vomiting stopped, no side effects
D. J.	41 y.	M		Digitalis intoxication	Vomiting	5 mg i.m. q 4 h for 2 days	Vomiting stopped, patient drowsy
J. W.	62 y.	M		Peptic ulcer	Vomiting 2 days	5 mg i.m. q 4 h for 1 day	Vomiting stopped, no side effects
C. L.	21 y.	F	64	Bronchial asthma	Vomiting 1 day	5 mg i.m.	Vomiting stopped, no side effects
L. H.	53 y.	M		Pneumonia	Hiccough 1 day	5 mg i.m. q 8 h for 2 days	No response
W. N.	52 y.	M	67	Uremia	Vomiting 1 week	5 mg p.o.	Vomiting stopped, no side effects
S. B.	36 y.	F	60	Gastroenteritis	Vomiting 1 day	10 mg p.o.	No effect
L. B.	35 y.	M	90	Gastroenteritis	Vomiting 1 day	20 mg p.o.	Suppression of vomiting for 3 h., no side effects
L. G.	24 y.	F	50	Psychogenic vomiting	Nausea 2 hours	10 mg p.o. followed by 20 mg p.o. in 1½ hours	Nausea and vomiting persisted. Patient felt weak and sleepy
L. G.	24 y.	F	50	Psychogenic vomiting	Vomiting 2 hours	5 mg suppository	Vomiting stopped; transient urge to defecate
U. U.	23 y.	F	68	Pregnancy	Vomiting 3 hours	5 mg suppository	Vomiting stopped; transient urge to defecate, slept 12 h.
D. J.	16 y.	M	60	Nephrotic syndrome	Nitrogen mustard 0.1 mg/Kg i.v.	40 mg p.o.	No vomiting, slept 10 h.
					Nitrogen mustard 0.1 mg/Kg i.v.	40 mg p.o.	No vomiting, slept 10 h.
					Nitrogen mustard 0.1 mg/Kg i.v.	20 mg p.o.	No vomiting, slight drowsiness
					Nitrogen mustard 0.1 mg/Kg i.v.	10 mg p.o.	No vomiting, no drowsiness
L. B.	35 y.	M	90	Gastroenteritis	Nausea, ½ hour	10 mg p.o.	Nausea relieved, no side effects

being carried out by several investigators. If antiemetic activity can be exhibited at lower doses, it may be possible to avoid some of the side effects.

Recently a new drug in this series, pipamazine (Mornidine®) was introduced for clinical evaluation. It possesses the antiemetic effect of the others, but in preliminary studies shows a lack of toxicity. It is chemically designated as 10-[3-(4 carbamoyl piperidino)-propyl]-2-chlorophenothiazine, and has the structural formula shown in figure 1.

Clinical Materials and Methods

Observations on 31 patients were carried out jointly at Children's Hospital and D. C. General Hospital. The drug was given to 17 children and 14 adults, ranging in age from 7 months to 62 years. There were 18 male and 13 female patients. The group included 8 patients with the nephrotic syndrome who were being treated with nitrogen mustard. The remainder were patients with nausea and/or vomiting, the result of diverse causes (table 1); one patient had singultus. The drug was usually given in 5 mg. and 10 mg. doses orally. Whenever necessary, this dosage was repeated at four or eight hour intervals. For the more acute cases the drug was administered intramuscularly; rectal suppositories containing 5 mg. were also employed. Patients who vomited following the initial dose of nitrogen mustard were given pipamazine simultaneously with the mustard therapy on the three following days. The other patients in the study were given the antiemetic drug on admission or during their hospital stay, as circum stances indicated.

Results and Comment

Table 1 presents data on the administration of pipamazine to 31 patients. This study demonstrated definite antiemetic properties of pipamazine at dose levels one fifth those of chlorpromazine. It was well tolerated when given orally, intramuscularly or rectally. The sedative effect is minimal. One 16 year old patient given 40 mg. orally slept for 10 hours without any untoward effects. Eight additional patients manifested slight drowsiness; the remainder showed none. Pipamazine provided dramatic relief from the nausea and vomiting of nitrogen mustard in patients previously shown to be susceptible to the strong vomiting stimulus of this compound. These patients therefore provided a relatively objective criterion for judging the effect of the drug. In the remainder of the patients, the clinical evaluation of the investigator, although not strictly controlled, bore out the impression of effective antiemetic properties. No untoward reactions were noted in this study.

SUMMARY

Pipamazine, a derivative of phenothiazine, was clinically evaluated as an antiemetic in 31 patients. A satisfactory antiemetic effect in doses one fifth those of chlorpromazine was obtained with minimal or no sedative effect. The drug was well tolerated in all patients, including infants, and afforded a wide margin of safety when used orally, intramuscularly or rectally.

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Clinical Note

Recent work has confirmed the previous reports that sarcomas develop in the rat at the site of intramuscular injection of the iron dextran complex "Imferon." As yet, there is no evidence that this drug is actually a hazard to man. However, as stated in the British Medical Journal, March 12, 1960, "The existing evidence is certainly sufficient to warrant, and indeed to demand, its speedy withdrawal from any kind of general use in man." Apparently producers of this drug in the United States are voluntarily withdrawing its sale until further investigations are completed, although the Food and Drug Administration has not made any positive recommendation.

In view of the above, no iron dextran complex shall be used on any staff patient of Children's Hospital without definite review for indications by the physician-in-chief. This is not an emergency drug in any instance. Thus, it will probably not be used at all until there is further information available.

The Editor's Column

THE LIMPING CHILD

Limp is relatively common in children. At times limp is insidious in its onset and not associated with pain, but more often pain is a concomitant complaint in the limping child. The causes of limp are many; from the anatomical viewpoint, any condition affecting the hip, pelvis, or lower spine may be a causative factor. *Inequality of leg length* without any restriction of joint motion will cause a limp. The limp also may be secondary to trauma, or a developmental or infectious process involving the hip, knee, or ankle. The child with a limp should not be permitted to bear weight until the cause of the limp has been definitely established.

The factor of *trauma* must always be considered in any child with a limp, since children in their everyday activities find many opportunities to injure the lower extremities or spine. The persistence of a limp justifies taking additional roentgenographic views, as often a minimal hairline fracture will not be recognized at the time of the initial roentgenogram.

Muscle atrophy, which may be determined by measuring the circumference of both the thigh and the calf of both lower extremities, is a helpful adjunct in evaluating the cause of a limp.

The persistence of a limp in a child should not be ignored, and careful examination may reveal a condition involving the 1) back; 2) hip; 3) knee; or 4) ankle and foot.

The hip: Any condition bringing about a mechanical instability of the hip joint will cause a limp. *Dislocation* of the hip or dysplasia of the hip will be manifested by a limp on the affected side when the child begins to walk. If the condition is bilateral and the child "limps on both sides," the diagnosis may be missed. *Congenital coxa vara,* the loss of the normal neck-shaft angle, will also cause a limp. *Osteochondritis* of the head of the femur (Legg-Perthe's disease) in the age group from 3 to 10 years is almost invariably associated with a limp. Local tenderness over the hip associated with limitation of internal rotation in both extension and flexion of the hip are concomitant objective physical findings. *Transient synovitis* of undetermined etiology is associated with limp. Frequently the etiology of the synovitis is never determined; the laboratory findings do not substantiate any appreciable increase in the white blood count or the sedimentation rate. In contrast to Legg-Perthe's disease, the history usually is of a relatively short duration. Often the presenting complaint on the part of the patient is pain in the region of the knee; this is the result of irritation of the obturator nerve, and pain distribution occurs over the anteromedial aspect of the lower thigh and knee. The complaint of pain about the knee in a child whose knee does not reveal any abnormality must be considered suggestive of some difficulty about the hip on the same side. *Early slipping of the upper femoral epiphysis* in the adolescent is another of the many causes of limp attributed to hip disorders. This is felt to be due to endocrine imbalance, although the etiology is undetermined. Initial roentgenograms are usually negative, but serial x-rays will show slight widening and irregularity of the capital epiphysis of the femur. There is associated an external rotation deformity and limitation of internal rotation in the early stages of the disease.

Any *neoplasm* about the ilium, or head, neck, or upper part of the femur will be characterized by a limp. The slowly progressing cystic group of lesions, such as eosinophilic granuloma, simple cysts, etc., will cause a limp. In addition any *infectious lesion,* such as tuberculosis, will be associated with a "hip limp."

The knee: Limp attributed to some pathologic change within or about the knee can usually be differentiated from limp caused by a hip or ankle condition. A *discoid cartilage, osteochondritis dissecans,* or *intra-articular synovial tumors* will cause a limp. Any involvement of an epiphysis about the knee, such as occurs in *osteochondritis of the tibial tuberosity* (Osgood Schlatter's disease), is another cause of limp.

The foot and ankle: Any disturbance in the mechanical efficiency of the

foot and ankle resulting in a *chronic sprain of the ligaments* may cause a limp. *Tibial torsion*, with the associated turning in of the ankle and foot, *forefoot adduction*, *primus metatarsus varus* and *talipes equinovarus* are but a few of the many gross deformities causing a limp. The *congenital tarsal coalitions*, manifested by an actual connecting bar of bone between the os calcis and talus or the os calcis and navicular bones, will cause a spastic type of flat foot with resulting limp. *Apophysitis of the os calcis* (Sever's disease), *osteochondritis of the tarsal scaphoid* (Kohler's disease), and *osteochondritis of the metatarsal head* (Freiberg's disease), as well as any other involvement of the epiphyses about the ankle and foot, can and often do precipitate a limp.

Among the neurological causes of limp are: 1) *spinal cord tumor*; 2) *unrecognized poliomyelitis* affecting some of the muscles of the lower extremities or back; 3) *muscular dystrophy*; and 4) *progressive muscular atrophy*.

The above comments are only suggestive of the many causes of limp in a child. Lastly, one occasionally sees a child who limps with his shoes on, but not with his shoes off. The embarrassing causative factor of the limp is frequently found to be a tack or some other rough surface in the shoe which simply causes the child to limp only when he wears his shoes.

W. J. T.

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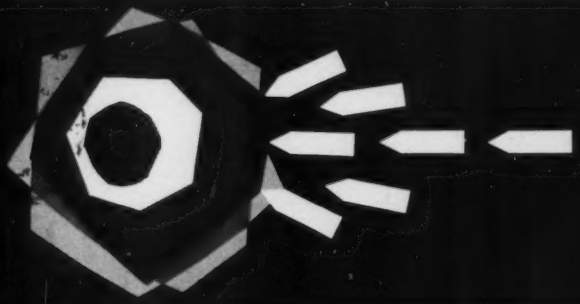

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Tacaryl possesses inherent long-acting properties. After rapid disappearance from the blood stream, Tacaryl is bound to the tissues. This protective affinity for tissue provides a notably sustained effect which does not depend upon the use of artificial, long-acting construction. The sustained action, an inherent property of the molecule, lasts for periods up to 12 hours.

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Tacaryl is absorbed quickly to provide relief of symptoms within an hour.

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In studies to date,[1] side effects were minimal; in a small percentage of patients, mild drowsiness was observed. Tolerance was not reported even after long usage. No cumulative effect has been observed.

clinically proved

In studies of 459 patients,[1] Tacaryl provided effective symptomatic relief in a wide variety of conditions, including allergic rhinitis, pruritus, various skin disorders, allergic bronchial asthma, pruritus of chickenpox, and allergic conjunctivitis. In some cases, the relief of itching bordered on the dramatic.[2] In a double-blind clinical evaluation[3] of various antihistaminic agents in hay fever, Tacaryl provided benefits in all patients with moderate to severe symptoms.

dosage: *adults*—One tablet (8 mg.) or two 5 cc. teaspoonfuls syrup (8 mg.) twice daily. *children*—One-half tablet (4 mg.) or one 5 cc. teaspoonful syrup (4 mg.) twice daily.

In some cases it may be desirable to adjust dosage to meet individual requirements.

supply: Scored tablets, 8 mg., bottles of 100. Syrup, 4 mg. per 5 cc. teaspoonful, 16 oz. bottles.

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